# Epidemiological Analysis for Outbreak Control

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Throughout history infectious disease has been a major cause of death, disability, and suffering. Disease control in recent times is based on a rational understanding of the patterns, causes, and effects of infectious disease and has been essential to the reduction of death and disability rates to less than 10% of historical rates in the last century in the US [1]. Striking examples of the power of rational techniques are the effective extinction of the organisms responsible for smallpox and rinderpest. The obvious question is the reach of these powerful techniques for solving other similar infectious disease problems. The emergence of the H1N1 pandemic influenza in 1918 is still not universally understood as a prime example of the damage that an emerging disease can cause. This raises the question whether there are rational methods that can help mitigate or even extinguish an emerging disease before it reaches the scope of smallpox, rinderpest, the 1918 pandemic influenza, or HIV disease. Analytical methods do exist—as those that allowed prediction of the control of severe acute respiratory syndrome (SARS) and estimated the level of contagion from the H5N1 bird-flu and 2009 pandemic influenza demonstrate. These promising developments show a path toward the use of rational interventions to improve the control of novel disease outbreaks.

The rational study of patterns, causes and effects of infectious disease is known as epidemiology. For contagious disease–a subset of infectious disease–that study often focuses on understanding the dynamics of how the disease propagates within a defined population, determining how fast it spreads, estimating the total number of infected individuals, and predicting the impact of prophylactic measures. Field and theoretical epidemiology played essential roles in the elimination of smallpox and rinderpest, providing the basis for the allocation of the human effort and resources that made global eradication a tractable problem. Theoretical epidemiology showed great promise during the global 2003 SARS outbreak as a tool for determining when infection control and mitigation had slowed disease transmission sufficiently so that control of the outbreak could be achieved and for anticipating the final regional size of the outbreak.

Control of the SARS epidemic in 2003 was a signal event. The disease exhibited high lethality, showed every indication of becoming a global pandemic, and had spread sufficiently once control efforts commenced that there were serious doubts that control could be achieved and a pandemic averted. The vast majority of the effort required to control the SARS outbreak consisted of field epidemiology, contact tracing, barrier nursing, and a host of other established medical and public health techniques. These techniques averted a pandemic, but they did not provide a strong analytical basis for identifying whether and at what point in time control of the outbreak had been achieved, nor what the time frame and final case count were likely to be. A team at LANL [2], one of several in the world, was able, with adequate access to epidemiological case-count data, to demonstrate the point in time at which eventual control of the epidemic was likely for specific countries or regions. Because the public health infrastructure and methods of control differed so strongly between countries, global predictions in the context of a single modeling exercise were not feasible in 2003.

The remarkable success of the global public health effort in controlling SARS notwithstanding, serious limitations in the deterministic methods used to analyze case-count data were brought into sharp focus in 2003. The methods used during the SARS outbreak to predict the course of the epidemic were derived from relatively simple-to-analyze ordinary differential equations, related to the minimal mathematical model,

$$\frac{dS(t)}{dt} = -\beta\frac{S(t)I(t)}{N},$$
$$\frac{dI(t)}{dt} = +\beta\frac{S(t)I(t)}{N} - \gamma I(t),$$
$$\frac{dR(t)}{dt} = +\gamma I(t)$$

where $S(t)$ is the population of susceptible individuals at time $t$, $I$ and $R$ describe the population of infectious and recovered (or "removed") individuals, $\beta$ describes the chance of an infectious individual infecting a susceptible person, and $\gamma$ is the rate of recovery (or "removal") of infectious individuals. Generalizations of these equations were used in 2003 to predict 396 probable and suspected cases of SARS in Ontario,

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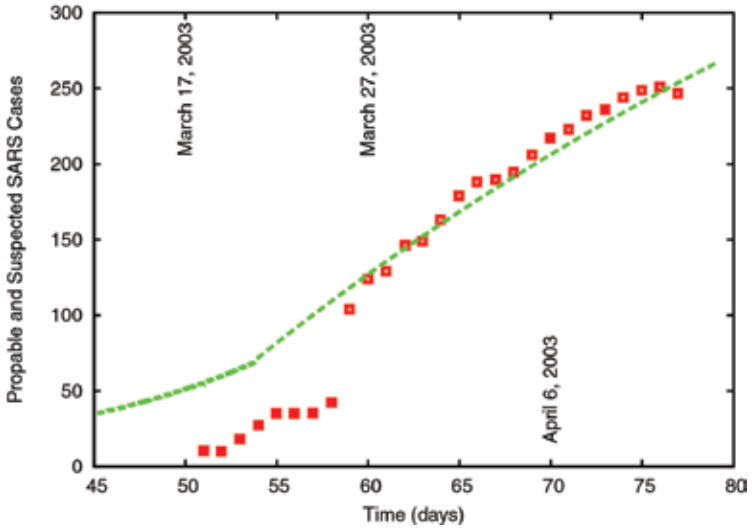


*Fig. 1. The cumulative number of probable and suspected Coronavirus SARS cases during the 2003 Ontario,Canada SARS outbreak. The jump in the data near day 60 reflects real-world reporting as knowledge of the situation improved. The green curve reflects a deterministic model accounting for the effects of variable diagnosis and patient isolation effects that change the transmission of the disease and alter epidemic progression. The kink in the green curve corresponds to the start of epidemic control measures by Canadian authorities. The model used to generate the green curve is a more complicated set of equations analogous to the simple susceptible, infectious, reeovered model discussed in the text. The green curve extrapolates to a final case count of 396 cases. The Canadian government reports 375 cases.*

while the actual result was 375 cases (247 probable cases and 128 suspected cases). Figure 1 shows the predictions made in 2003 using real-world non-ideal data [2]. While equations of this type provide a reasonable first approximation to the epidemic dynamics, they provide no statistical confidence or likelihood for their predictions.

The deterministic model of disease spread was adequate for making important predictions in the 2003 SARS outbreak, but the uncertainties in those predictions can only be estimated in an ad hoc way, and the model is the least reliable early in the outbreak when case counts are small and prospects for controlling the outbreak are best. Ideally, we would have a statistical measure of how likely an outbreak is to grow as an epidemic and what the likely growth rate is to help estimate the efficacy of disease control measures in real time. The human H5N1 "bird flu" outbreaks that have simmered for over a decade have resulted in several dozen confirmed deaths each year for most of the last decade. The reason these outbreaks result in locally confined outbreaks–not global pandemics–is that the virus has failed to achieve efficient person-to-person transmission. Using Bayesian statistical methods to generalize the deterministic equations to a probabilistic form, we can estimate the number of new cases caused by each current case. This allows us to estimate the range of potential epidemic growth rates most consistent with the observed case counts (Fig. 2) [3]. This technique is applicable even very early in an epidemic when case counts are small. This represents a significant advance in our ability to provide high-quality information on the effectiveness of disease control efforts to public health officials during a crisis. Knowing the range of potential growth rates means that a more realistic view of the possibility for epidemic growth can be achieved than the simple picture of "control/no control" that was available during the SARS outbreak.

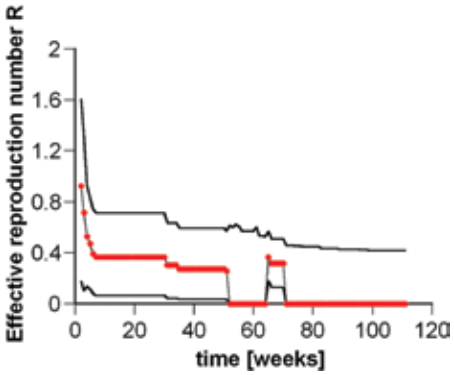


*Fig. 2. Sequential Bayesian estimation of the basic reproductive number R for H5N1 bird-influenza infecting people in Vietnam. The mean estimated value of R is shown in red, and the 95% credible interval lies between the upper and lower black curves. Values of R smaller than 1 indicate an outbreak is no longer viable and that spread will be self-limiting.*

[1] Centers for Disease Control, *Morbidity and Mortality Weekly Report* **48**, 621 (1999).

[2] Chowell, G. et al., *J Theor Biol* **224**, 1 (2003).

[3] Bettencourt, L.M.A. and R.M. Ribeiro, *PLoS One* **3**, e2185 (2008).